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Provisional Application Cover Sheet

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This is a request for filing a PROVISIONAL APPLICATION under 37 C.F.R. § 1.53(b)(2).

Docket Number: P3039	Type a plus sign (+) inside this box	+

Inventor(s)/Applicant(s)			
Last Name	First Name	Middle Initial	Residence (City and either State or Foreign Country)
Luzzi	David		Wallingford, PA

Title of the Invention (280 Characters Maximum)

BioMedical Applications of 1-D Systems

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Enclosed Application Parts (*check all that apply*)

[X] Specification *Number of pages*: 6 [ ] Small Entity Statement

[ ] Drawing(s) *Number of sheets*: [ ] Other (specify)

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The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

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[ ] Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

Signature: [signature]

Typed or Printed Name: David Luzzi

Date: 12/11/03

[ ] Additional inventors are being named on separately numbered sheets attached hereto.

PROVISIONAL APPLICATION FILING ONLY

PROVISIONAL APPLICATION SUBMISSION TO USPTO – CONTENTS PAGE

Penn Docket Number : P3039

First-named Inventor : Luzzi

Submission Date : 12/11/03

Prepared by : Matt Thomas

CONTENTS LISTED IN ORDER :

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Tech Disclosure 5 – BioMedical Applications of 1-D Systems
David E. Luzzi

Technological Need – This disclosure addresses three needs

1. Tools with which researchers can probe the interior of cells and other vesicular structures, introduce substances and remove substances with control and with minimal disruption of the vesicular structure.
   a. A benchmark for the case of cell analysis or modification would be the immediate survival of the cell, or an absence of direct lethal effect from the penetrating action of the probe.

2. Tools that provide effective tests of the efficacy of candidate therapeutic agents using human, or other, cells
   a. Providing separation of the delivery component of efficacy from the chemical interaction component of efficacy
   b. Providing ex-vivo, in-vitro, parallel testing on sufficient number of human cells such that the analysis is statistically relevant
   c. Requiring small volumes of therapeutic agent for analysis
   d. Providing rapid and effective screening of candidate therapeutic agents prior to the start of expensive pre-clinical and clinical testing.

3. Tools that provide effective tests for the presence of chemical interaction between candidate therapeutic agents, or test substances, and a particular disease-related, or other-condition-related, target substance, within a process of high-throughput screening either within human cells or within reaction vessels of appropriate type.

Cellular Probes as Tools for Biomedical Research on Single Cells or as Tools for Drug Discovery and Development
David E. Luzzi

This basic architecture provides the means to deliver two Nanotechnology solutions, one near term within 1-2 years and one longer term over 3-5 years.

A. Nanotechnology Solution 1: Single Cell Probes for Biomedical Research

This technology development effort aims to produce probes that will provide the capabilities to introduce small quantities of substance into a cell and/or the cell nucleus and to either leave this substance behind or remove the substance after controllable intervals. This delivery will be accomplished with minimal disruption of the lipid membrane of the cell or cell nucleus. The target is a technology in which a tool could be delivered to the customer that would allow the delivery of any specified substance into a cell or a section of a cell without killing the cell or damaging the cell to an experimentally-significant amount. Once the tool is obtained, then interchangeable functional probes would be an ongoing, disposable product.

The main driver for these ideas is the need for a more effective research solution for programs researching disease or injury processes (or chemical interaction processes) in which the ability to modify the interior of a cell without damaging the cell membranes is important.

The single cell probe concept does not require new scientific discovery. Rather it requires an engineering-based joining of existing technologies, possibly including some chemical reaction development (but the path is known). The technology is conceptualized as in Figure 1.

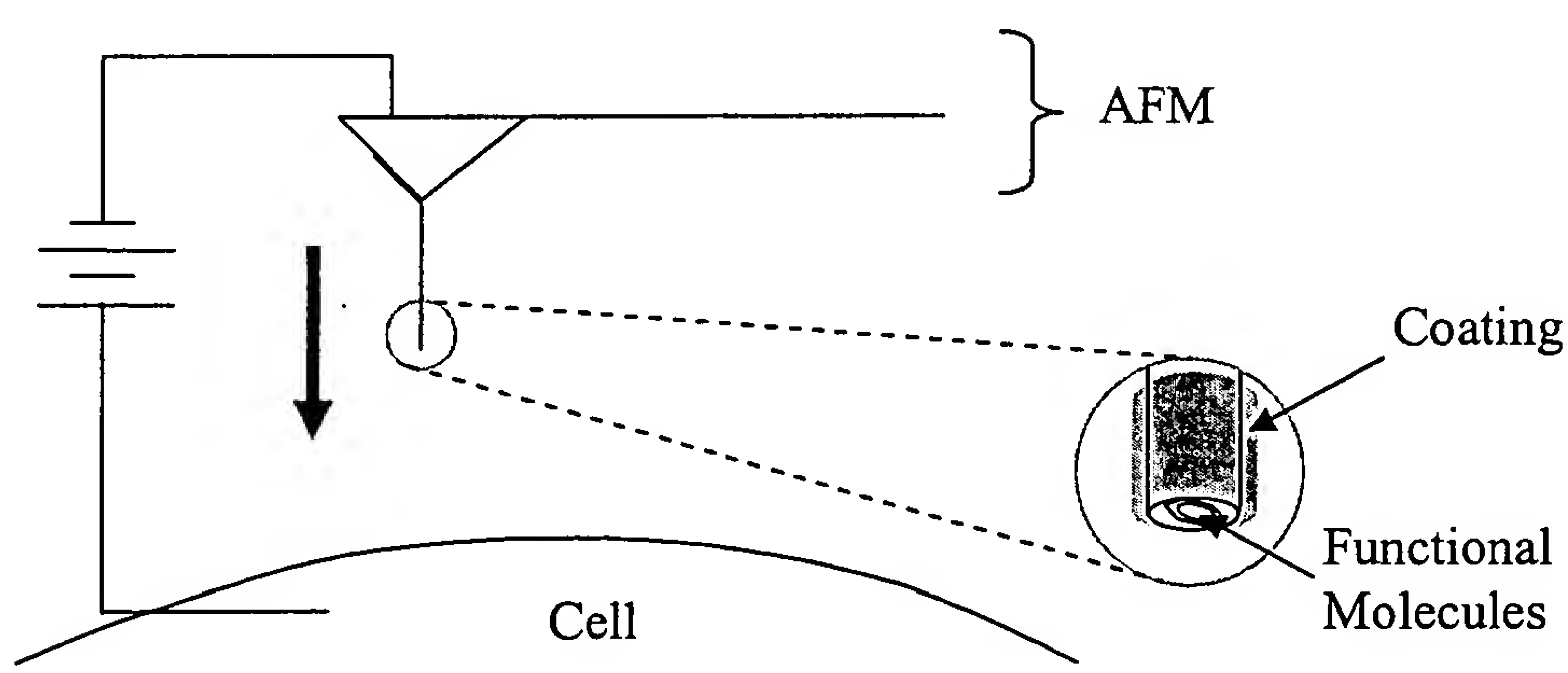

Figure 1

The system utilizes atomic force microscope (AFM) technology for force sensing and fine position of the probe, as well as the longitudinal penetration translations. Ultimately, only light microscopes and micron-resolved mechanical control may be necessary for a commercial research tool. The probe component is envisioned as a tubular or solid, high-aspect-ratio fiber with diameter between 1 and 100 nm. Such fibers are commercially

available and/or are produced in my laboratory. The functionality of the probe can be achieved in three ways.

1. Delivery of a substance from the interior of a tubular fiber. In this case the delivery is irreversible.
2. Delivery of a substance that is a component of a coating on the exterior side-walls and/or the tip of the probe.
3. Delivery of a substance that is covalently bonded to the exterior of the fiber through a chemically functional ligand.

For the first case, the development of fluidics at the sub-micron scale is required and will be part of the work associated with Nanotechnology solution 2. For the second case, two technologies are known for the production of bio-functional materials in which active enzymes are sterically-confined, yet active; one is a polymer-based composite, the other a sol-gel ceramic composite. The remaining technology development is the conversion of these bulk materials into coatings on the fibers, which could involve chemical reaction development. The third scheme involves the direct functionalization of the fiber surface with bio-active molecules via chemical ligands. Other potentially useful configurations of the system are the provision for an electrostatic potential between the probe and the cell interior (as seen in Figure 1) and/or the encapsulation of optically-emitting molecules (especially in the near-IR) within the lumen of tubular fibers as a means for probe location and optical stimulation of the cell.

The goal is to deliver a technological platform in which a wide variety of candidate enzymes or other substances can be provided in non-disruptive cellular probe architecture for controllable delivery to a cell. In terms of production, this technology would benefit from newly developed commercial methods to make large numbers of nanotube and nanofiber AFM probes through parallel processing.

Potential IP

1. Optical emitting molecules within nanotubes
2. Bio-functional coatings on nanotubes and/or nanofibers (Broad and specific)
3. The whole system
4. Device components for the delivery of a substance from inside a nanotube (driven nanofluidics or molecular/mass transport)
5. Specific bio-functional nanotubes or nanofibers

B. Nanotechnology Solution 2: Nanofiber and Nanotube Tools for Drug Development

A schematic of the current timeline of expenditures and revenue streams for pharmaceutical research is schematically shown in Figure 2. The three points at which Nanotechnology solutions could positively impact this process are indicated. In the early stages of research after a specific target has been identified, Nanotechnology can enable the reduction of volumes needed for testing of the proprietary compounds within a corporations library. The second positive impact is in the development of testing systems that would increase the probability that a candidate compound will fail early in testing before expensive pre-clinical and clinical trials are required. The third impact would be yet unidentified tools to accelerate the completion of trials to allow for a quicker product launch.

The concept here is to produce integrated versions of Nanotechnology Solution 1 in which parallel nano-fluidic devices provide economies of scale, reduction in process costs, and/or separation of the components of drug efficacy for superior testing. In the solutions to Goals 1 and 2 of Figure 2, devices would be created in which nanotubes from 1 to 100 nm are assembled through a substrate acting as probes (pipettes). On one side, the nanotubes would be connected to one or more reservoirs. On-chip lithographic patterned or self-assembled components would provide the electronic, local electromagnetic, magnetic, mechanical, and/or optical drive to "pump" atoms, molecules, materials or fluids (drive the mass transport) through the nanotubes.

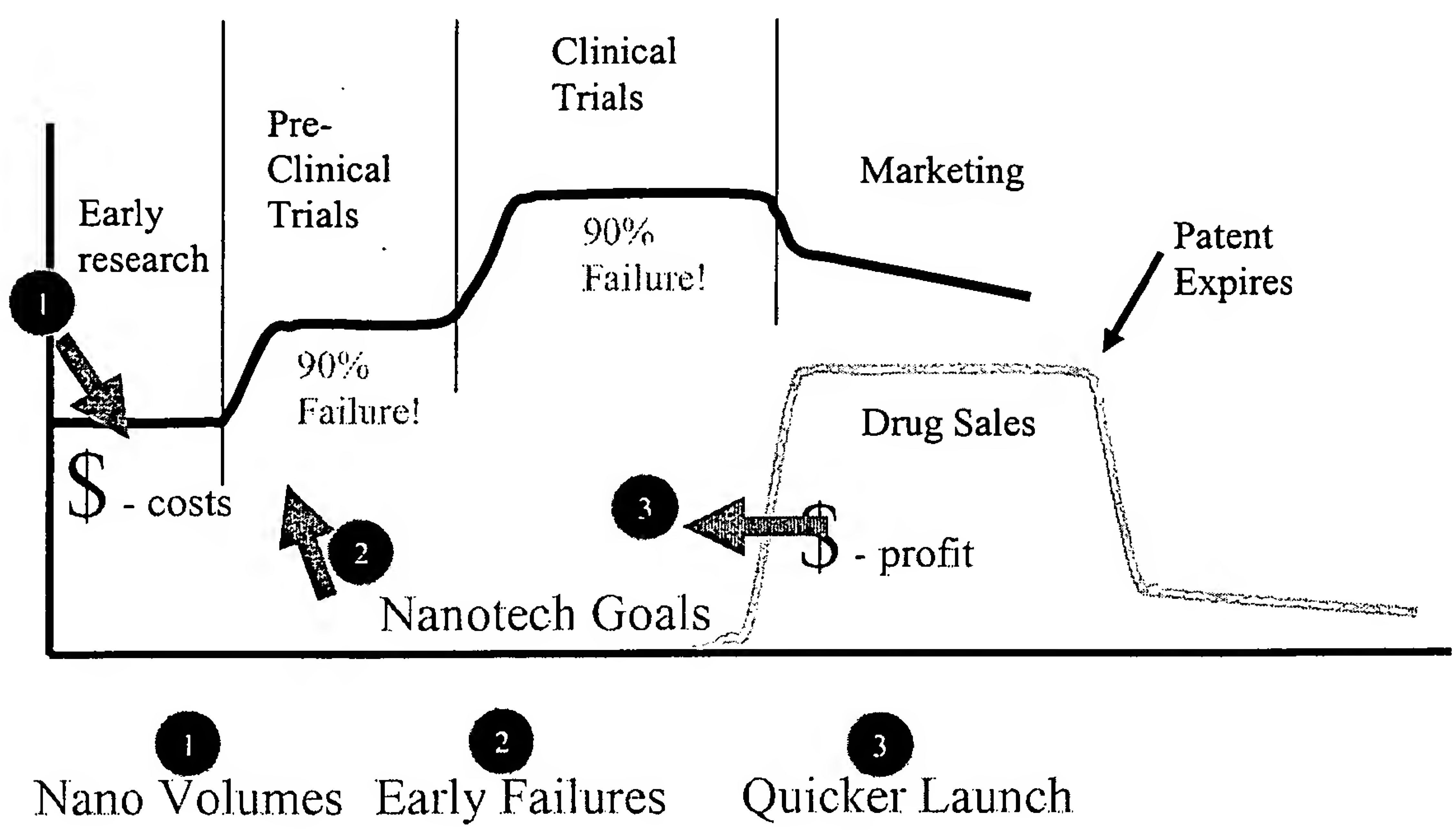

Figure 2

In one manifestation most likely for Goal 1, the device will access separate reservoirs of analytes for rapid trial using small volumes of analyte for the testing of chemical interactions with target molecules or bio-molecules. These analytes would most likely be the chemical compounds in the corporate chemical library. In another manifestation most likely for Goal 2, a device of parallel nano-fluidic channels is used to deliver a single candidate therapeutic (one large reservoir) to the interior of a plate of cells (human, animal, or plant). Each probe would insert into a different cell as designed-in by the spacing of the probes in the device. A large number of cells, potentially in the thousands could be treated in one application. This device could be combined with functional cell substrates that provide topographic or chemical functionalization to control the orientation of each cell allowing the insertion of the probe in similar locations in every cell. This device would allow a statistical analysis of the interaction between the injected chemical and the cell. This device also provides for the separation of the efficacy of delivery of the chemical through the lipid membrane (or cell membrane or nuclear membrane) from the efficacy associated with the bio-chemical interaction of the chemical with its target in the environment of the cell.